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Title Page

Assessment of Breathlessness in Lung Cancer: Psychometric Properties of the Dyspnoea-12 Questionnaire

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Assessment of Breathlessness in Lung Cancer: Psychometric Properties of the Dyspnoea-12 Questionnaire

Abstract

Content: The Dyspnoea-12 (D-12) is a well validated instrument in respiratory illnesses for breathlessness assessment, but its psychometric properties have not been tested in lung cancer.

Objectives: To demonstrate the psychometric properties of the D-12 in lung cancer patients.

Methods: Baseline data from a lung cancer feasibility trial were adopted for this analysis. D-12 and a series of patient-reported tools including five Numeric Rating Scales (NRS), the Hospital Anxiety and Depression Scale (HADS) and the Lung Cancer Symptom Scale (LCSS) were employed for the psychometric assessment. Spearman's correlation coefficients (r_s) were used to estimate the convergent validity of the D-12 with the NRS, HADS and LCSS. Exploratory factor analysis was performed to examine construct validity. Reliability was tested by Cronbach's alpha and item-to-total correlations. D-12 score difference between patients with or without anxiety, depression and COPD was explored to identify its discriminate performance.

Results: One hundred and one lung cancer patients were included. There were significantly positive correlations between the D-12 and the HADS, LCSS, and NRS scales measuring the breathlessness severity and its associated affective distress. Factor analysis clearly identified two components (physical and emotional) of the D-12. Cronbach's alpha for D-12 total, physical and emotional subscales was 0.95, 0.92 and 0.94, respectively. Patients with anxiety or depression demonstrated significantly higher D-12 scores than those without it, and patients with COPD reported significantly more severe breathlessness than those without COPD.

Conclusion: The D-12 is a valid and reliable self-reported questionnaire for use in breathlessness assessment in lung cancer patients.

Key Words

Breathlessness; Lung cancer; Scale; Psychometrics; Validity; Reliability

Running title

Validation of the Dyspnoea-12 in Lung Cancer

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Introduction

Breathlessness is defined as "a subjective experience of breathing discomfort that consists of qualitatively distinct sensations that vary in intensity" [1]. It is one of the most distressing symptoms frequently identified in lung cancer [2-5]. Evidence supports breathlessness as a multidimensional experience, as the presence of breathlessness is associated with physical and emotional distress such as fatigue, anxiety, depression, and deterioration of quality of life (QoL) [2, 5, 6]. As breathlessness is a subjective symptom involving both physical and psychological factors, its measurement should be multidimensional using patient-reported approaches that encompass its different dimensions [1, 7].

There is a plethora of instruments for assessing breathlessness, although most of them have been validated for chronic obstructive pulmonary disease (COPD) [8]. Commonest used unidimensional tools for breathlessness assessment include the modified Borg scale, visual analogue scale (VAS) and numerical rating scale (NRS) [8, 9]. Although these tools are easy to complete, the use of different endpoints makes it difficult to do comparisons between studies [8], and their unidimensional nature requires the use of multiple instruments to obtain a full understanding of breathlessness. The Medical Research Council (MRC) dyspnoea scale is also a popular tool for grading breathlessness [8]. However, it is only activity-specific and it is weak in its association with patients' physiological and functional distress, which make it impossible to use for the multidimensional assessment of breathlessness [8, 10].

Multidimensional instruments for breathlessness assessment have been introduced, such as the Cancer Dyspnoea Scale (CDS) [11-13]. But the CDS only includes the anxiety as patients' psychological distress and the evidence in terms of its responsiveness and minimal clinically important difference (MCID) is lacking [11-14]. The Chronic Respiratory Questionnaire (CRQ) is a good candidate for breathlessness assessment [14]. It has been well validated in chronic respiratory diseases such as COPD and interstitial lung disease (ILD) [14], and the psychometric properties of its short form have also been preliminarily identified in lung cancer [15]. However, the patient may take a relatively long time to complete the entire CRQ, and small changes in breathlessness may not be captured by repeated administration of the CRQ [16, 17]. Another tool named Breathlessness Assessment Guide has also been developed for lung cancer without any psychometric testing [18, 19]. There is a shortage of instruments that could be used for measuring breathlessness among different advanced diseases [8].

The Dyspnoea-12 (D-12) is a convenient patient-reported scale for measuring the severity of breathlessness [20]. Breathlessness is quantified by using 12 descriptors to cover both its physical and psychological dimensions [20]. The D-12 has established its validity and reliability in COPD [20], asthma [21], ILD [22] and pulmonary hypertension [23], but its psychometric properties have not yet been assessed in lung cancer. Therefore, the aim of this study was to determine the validity and reliability of the D-12 in lung cancer, by using data from a recent lung cancer feasibility randomised controlled trial (RCT) [24].

Materials and Methods

Research ethical approval was granted to this study, and research governance approval was also received from the study hospitals. All participants provided written informed consent.

Overview of the Feasibility Trial

This was a multi-centre feasibility RCT conducted in the UK [24]. It aimed to feasibility test a non-pharmacological intervention for managing the lung cancer respiratory distress symptom cluster (breathlessness-cough-fatigue). The intervention consisted of a couple of self-management approaches such as the techniques for breathing control, cough easing and self-acupressure [24]. A total of 107 lung cancer patients joined the study and 101 were included in the analysis. Participants completed self-reported outcome measures including a range of scales to assess symptoms, psychological distress and QoL [24]. In the current study, only baseline data were used for analysis.

Study Instruments

The most pertinent outcome measures for examining the D-12 psychometric properties were included in this analysis.

-Dyspnoea-12 Questionnaire (D-12)

The D-12 uses 12 items to generate a global assessment of the severity of breathlessness [20]. Each item is rated on a 4-point Likert scale from 0 (none) to 3 (severe), and the total scores range from 0 to 36 with a higher score indicating more severe dyspnoea [21-23]. Items 1 to 7 are summed up to create the physical component score, and items 8 to 12 are used for calculating the emotional component score [21, 23]. MCID of the D-12 has been determined in the feasibility trial using anchor-based and distribution-based methods, with a value of 3 units [24].

-NRS Breathlessness Scales

Five 0-10-point NRS scales were adopted to measure the average and worst breathlessness experienced during the past 24 hours (higher scores=worse conditions), breathlessness-related unpleasantness and distress (higher scores=worse conditions), and patients' ability to cope with breathlessness (higher scores=better conditions) [24-26]. The NRS scales were used to explore the associations with the D-12 total and component scores.

-Hospital Anxiety and Depression Scale (HADS)

The HADS is a 14-item self-reported instrument for determining the general state of psychological distress, with seven items each assessing anxiety and depression respectively [27, 28]. Each item is rated from 0 to 3, thus the scores for either anxiety or depression scale range from 0 to 21 (higher scores=more severe outcomes) [27, 28]. For particular statistical purpose, a HADS anxiety score (HADS-A) of 8.0 or above was suggested as the presence of anxiety while a HADS depression score (HADS-D) of 8.0 or above was indicated as the presence of depression [28, 29]. The HADS was employed to explore the association with the D-12 as they both contain an emotional content for measuring psychological distress.

-Lung Cancer Symptom Scale (LCSS)

The LCSS is a QoL assessment tool with well documented psychometric properties [30, 31]. The LCSS patient-reported scale consists of nine items with six assessing prominent symptoms related to lung cancer and another three evaluating patients' "symptomatic distress", "activity status" and "overall QoL" [30]. All items use the 0-100 VAS scale (higher scores=worse outcomes) and the total score is computed as the mean of all the nine items [32]. The LCSS was used to explore its correlations with the D-12 as QoL in lung cancer has been proved to be negatively associated with dyspnoea [5].

Psychometric Assessment

-Reliability and Validity

Internal consistency reliability for the D-12 was examined and the item-to-total correlations were adopted to explore the relationships between one single D-12 item score and the total D-12 score without that item [33]. Validity was examined by convergent validity and construct validity. Convergent validity is estimated by examining "whether the measured variables correlate with other measures of the same concept" [34]. Associations between the D-12 and the NRS, HADS and LCSS were explored to identify the D-12 convergent validity. Exploratory factor analysis (EFA) was applied to estimate the D-12 construct validity.

-Acceptability, Floor and Ceiling Effects, Invariance and Discriminate Performance

Acceptability of the D-12 was estimated by calculating the percentage of missing value across all the D-12 items. Percentages of the subjects who had the lowest and highest possible D-12 total score were computed respectively to estimate the floor and ceiling effects of the D-12. Invariance of the D-12 was tested for age and gender factors. Discriminate performance analyses were considered for subjects with or without anxiety, depression and COPD.

Statistical Analysis

The IBM SPSS Statistics for Windows version 22.0 (IBM Corp, Armonk, NY, USA) was adopted for data analysis with the statistical significance setting as $P<0.05$. Descriptive statistics were presented to summarise patients' demographic data, acceptability, and the floor and ceiling effects of the D-12. Spearman's correlation coefficients (r_s) were adopted for exploring the associations between the D-12 and the NRS, HADS and LCSS, as most of the instrument scores in our sample violated the assumption of normal distribution. Principal component analysis (PCA) with a varimax rotation (eigenvalues >1) was used for the EFA. Items that loaded >0.6 were retrieved for a potential factor.

Independent-samples t-test or Mann-Whitney U test (as determined by the normality test) was adopted to estimate the D-12 score difference in different subgroups (e.g. anxious vs. not anxious, and COPD vs. non-COPD). Age difference was analysed by exploring the association (r_s) between the D-12 and patients' age. Internal consistency was estimated by Cronbach's alpha, and an alpha score of 0.8 or above is determined as very good for an instrument [35]. An item-to-total correlation is viewed as adequate once the value reaches 0.4 [36].

Results

Patients' Demographic and Clinical Data

One hundred and one participants were included. The majority of the patients were aged over 60 years old and had dyspnoea. Around one third of them presented anxiety or depression (**Table 1**).

D-12 Descriptive Analysis

The mean score for D-12 total was 17.8 (SD=9.4), and it was 11.0 (SD=5.3) and 6.6 (SD=4.8) for D-12 physical and D-12 emotional subscale, respectively **(Figure 1)**. Missing values within the D-12 were identified in no more than four subjects for each item across items 1 to 8. No missing data were detected for items 9 to 12. Proportions of the patients with the lowest (0) and possibly highest score (as of 35 in this sample) of the D-12 total were 4.0% (4/101) and 1.0% (1/101), respectively.

D-12 Convergent Validity

D-12 scores were strongly and positively correlated with HADS and LCSS scores (all at $P<0.001$). The highest r_s was identified between D-12 emotional subscale and HADS anxiety subscale ($r_s=0.71$, $P<0.001$). Significantly positive correlations can be found between D-12 and NRS "average" and "worst" breathlessness, and "distress" and "unpleasantness" associated with breathlessness (r_s

ranged from 0.48 to 0.64, all at $P<0.001$). Slightly negative (but insignificant) correlations were shown between D-12 and NRS "ability to cope with breathlessness" ($P>0.05$) (**Table 2**).

D-12 Construct Validity

There were two well-defined factors with items 1 to 7 clustering around the first factor (coefficients ranged from 0.68 to 0.81, representing the physical dimension of breathlessness) and items 8 to 12 gathering around the second factor (coefficients ranged from 0.78 to 0.87, indicating the emotional dimension of breathlessness) (**Table 3**).

D-12 Reliability

Internal consistency of the entire D-12 questionnaire was already reported in the feasibility study paper, with the Cronbach's alpha of 0.95 [24]. Internal consistency for the D-12 physical and emotional subscales was also excellent, with Cronbach's alpha being 0.92 and 0.94, respectively. Adequate item-to-total correlations of the D-12 were identified, with the coefficients ranging from 0.59 to 0.84 (mean 0.8).

D-12 Invariance and Discriminate Performance

There was no difference in D-12 scores between male and female patients (all at $P>0.05$), and Spearman's correlation also showed no association between D-12 and age (r_s ranged from -0.15 to -0.12, all at $P>0.05$). Patients with anxiety or depression presented significantly higher D-12 scores than those without anxiety or depression (all at $P<0.001$) (**Table 4**). Similarly, patients with COPD also had significantly higher D-12 scores than non-COPD patients (all at $P<0.05$, **Table 5**).

Discussion

The D-12 is a short scale confirming earlier reports in non-cancer populations that has minimal missing data [23]. Acceptability of the D-12 was documented, as missing values across items and the floor and ceiling effects were minimal in the lung cancer sample. Given the good completion rate of the D-12 and its ability to gain an overall score that incorporates multidimensional aspects of dyspnoea severity, the clinical utility of the D-12 seems promising.

Convergent validity of the D-12 was adequate. The significantly positive associations between the D-12 and the NRS scales indicated the possibility of using one single instrument instead of multiple tools to measure the overall severity of breathlessness. There was a negative (but insignificant) correlation between the D-12 and patients' coping ability, which indicted that severe dyspnoea might impair the patients' ability to cope with the symptom. However, it is also suggested that the distress induced by the symptoms emotional component might, in turn, motivate patients' behaviour [21]. The potentially bidirectional function of psychological distress might partially contribute to the above insignificant correlation. As coping ability is a complex construct which is almost impossible to capture in a single item scale, its relationship with dyspnoea is worthy of further exploration.

The D-12 was strongly correlated with anxiety and depression, as both the HADS and D-12 possess the psychological construct that measures patients' emotional status. Theoretically, D-12 emotional subscale would be expected to correlate more strongly with the HADS than the D-12 physical subscale, and this assumption was precisely captured in our findings. Similar to our previous findings [21-23], correlations between D-12 and HADS were only moderate. This suggested the difference of the focus of emotional distress between D-12 and HADS, with the former capturing the emotional status related to dyspnoea and the latter focusing more on the general status of emotional problems [23].

Breathlessness is a negative predictor of QoL in lung cancer [2, 5, 37], and this was sensitively captured by the D-12 as significant correlations were shown between D-12 and LCSS. Factor analysis supported very good construct validity of the D-12, which was highly consistent with the factor analysis result during the development stage of the D-12 [20].

It is not surprising that no gender and age difference was detected across D-12 scores, as age and gender have been reported not to be related to dyspnoea in lung cancer [6]. Also, during the D-12 development stage, items with gender or age bias had already been abandoned [20, 22]. Patients with anxiety or depression experienced more severe dyspnoea than those without such affective distress, as expected, because emotional problems such as anxiety and depression have been noted to be closely associated with breathlessness distress in lung cancer [6, 38, 39].

Breathlessness is one of the leading symptoms in COPD [40, 41]. COPD patients tend to experience similar or more severe dyspnoea and impaired QoL than that in lung cancer patients at a comparable advanced disease stage [42-44]. Lung cancer patients with COPD are expected to experience more severe dyspnoea than those without COPD, and this was accurately captured by the D-12 as patients with COPD had significantly higher D-12 scores than non-COPD patients.

The study has some limitations. Sample size estimation in the feasibility trial was not powered for the purpose of estimating psychometric properties. The D-12 scores in the control group subjects were not appropriate for estimating test-retest reliability because there was not a suitable anchor from the outcome measures that can be used to ensure patients' stability over time. D-12 divergent validity was also not performed due to the absence of available data. Despite these limitations, our study demonstrated that the D-12 is a valid and reliable assessment for breathlessness in lung cancer. Given its MCID was also identified [24], the D-12 can be a good option for use in future lung cancer trials to measure patients' breathlessness severity. Also, psychometric properties of the D-12 in lung cancer are consistent with previous validation studies in other respiratory diseases [20-23], which indicates its promising role for measuring breathlessness in a wide range of conditions.

Conclusion

D-12 is a valid and reliable patient-reported instrument for measuring breathlessness in patients with lung cancer. Future lung cancer studies are encouraged to adopt the D-12 as one of the outcome measures for breathlessness assessment.

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References

[1] American Thoracic Society. Dyspnea: mechanisms, assessment, and management. A consensus statement. Am J Respir Crit Care Med, 1999; 159:321-340.

[2] Smith EL, Hann DM, Ahles TA, et al. Dyspnea, anxiety, body consciousness, and quality of life in patients with lung cancer. J Pain Symptom Manage, 2001; 21(4), 323-329.

[3] Molassiotis A, Lowe M, Blackhall F, Lorigan P. A qualitative exploration of a respiratory distress symptom cluster in lung cancer: cough, breathlessness and fatigue. Lung Cancer, 2011; 71(1), 94-102.

[4] Dudgeon DJ, Kristjanson L, Sloan JA, Lertzman M, Clement K. Dyspnea in cancer patients: prevalence and associated factors. J Pain Symptom Manage, 2001; 21(2), 95-102.

[5]Iyer S, Taylor-Stokes G, Roughley A. Symptom burden and quality of life in advanced non-small cell lung cancer patients in France and Germany. Lung Cancer, 2013; 81(2), 288-293.

[6] Henoch I, Bergman B, Gustafsson M, Gaston-Johansson F, Danielson E. Dyspnea experience in patients with lung cancer in palliative care. Eur J Oncol Nurs, 2008; 12(2), 86-96.

[7] Parshall MB, Schwartzstein RM, Adams L, et al. An official American Thoracic Society statement: update on the mechanisms, assessment, and management of dyspnea. Am J Respir Crit Care Med, 2012; 185(4): 435-452.

[8] Bausewein C, Farquhar M, Booth S, Gysels M, Higginson IJ. Measurement of breathlessness in advanced disease: a systematic review. Respir Med, 2007; 101(3), 399-410.

[9] Johnson MJ, Close L, Gillon SC, et al. Use of the modified Borg scale and numerical rating scale to measure chronic breathlessness: a pooled data analysis. Eur Respir J, 2016; doi: 10.1183/13993003.02089-2015.

[10] Chhabra SK, Gupta AK,Khuma MZ. Evaluation of three scales of dyspnea in chronic obstructive pulmonary disease. Ann Thorac Med, 2009; 4(3), 128-132.

[11] Tanaka K, Akechi T, Okuyama T, Nishiwaki Y, Uchitomi Y. Development and validation of the Cancer Dyspnoea Scale: a multidimensional, brief, self-rating scale. Br J Cancer, 2000; 82(4), 800-805.

[12]Uronis HE, Shelby RA, Currow DC. Assessment of the psychometric properties of an English version of the cancer dyspnea scale in people with advanced lung cancer. J Pain Symptom Manage, 2012; 44(5), 741-749.

[13] Henoch I, Bergman B, Gaston-Johansson F. Validation of a Swedish version of the Cancer Dyspnea Scale. J Pain Symptom Manage, 2006; 31(4), 353-361.

[14] Dorman S, Byrne A, Edwards A. Which measurement scales should we use to measure breathlessness in palliative care? A systematic review. Palliat Med, 2007; 1-27.

[15] Charalambous A, Molassiotis A. Preliminary validation and reliability of the Short Form Chronic Respiratory Disease Questionnaire in a lung cancer population. Eur J Cancer Care, 2015; doi: 10.1111/ecc.12418.

[16] Guyatt GH, Berman LB, Townsend M, Pugsley SO, Chambers LW. A measure of quality of life for clinical trials in chronic lung disease.1987; Thorax, 42(10), 773-778.

[17] Molen B. Dyspnoea: a study of measurement instruments for the assessment of dyspnoea and their application for patients with advanced cancer. J Adv Nurs, 1995; 22(5), 948-956.

[18] Corner J, O'Driscoll M. Development of a breathlessness assessment guide for use in palliative care. Palliat Med, 1999; 13(5), 375-384.

[19] Al-Ghabeesh S, Ahmad M. Unidimentional and multidimensional breathlessness specific instruments for adult population: Literature review. J Nat Sci Res, 2012; 2(8), 1-15.

[20] Yorke J, Moosavi SH, Shuldham C, Jones PW. Quantification of dyspnoea using descriptors: development and initial testing of the Dyspnoea-12. Thorax, 2010; 65(1), 21-26.

[21] Yorke J, Russell AM, Swigris J, et al. Assessment of dyspnea in asthma: validation of The Dyspnea-12. J Asthma, 2011; 48(6), 602-608.

[22] Yorke J, Swigris J, Russell AM.et al. Dyspnea-12 is a valid and reliable measure of breathlessness in patients with interstitial lung disease. Chest, 2011; 139(1), 159-164.

[23] Yorke J, Armstrong I. The assessment of breathlessness in pulmonary arterial hypertension: reliability and validity of the Dyspnoea-12. Eur J Cardiovasc Nurs, 2014; 13(6), 506-514.

[24] Yorke J, Lloyd-Williams M, Smith J, et al. Management of the respiratory distress symptom cluster in lung cancer: a randomised controlled feasibility trial. Support Care Cancer, 2015; 23(11), 3373-3384.

[25] Farquhar MC, Prevost AT, McCrone P, et al. Is a specialist breathlessness service more effective and cost-effective for patients with advanced cancer and their carers than standard care? Findings of a mixed-method randomised controlled trial. BMC Medicine, 2014; 12(1), 1.

[26] Barton R, English A, Nabb S, Rigby AS, Johnson MJ. A randomised trial of high vs low intensity training in breathing techniques for breathless patients with malignant lung disease: a feasibility study. Lung Cancer, 2010; 70(3), 313-319.

[27] Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand, 1983; 67(6), 361-370.

[28] Snaith RP. The hospital anxiety and depression scale. Health Qual Life Outcomes, 2003; 1(1), 1.

[29] Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale: an updated literature review. J Psychosom Res, 2002; 52(2), 69-77.

[30] Hollen PJ, Gralla RJ, Kris MG., et al. Measurement of quality of life in patients with lung cancer in multicenter trials of new therapies. Psychometric assessment of the Lung Cancer Symptom Scale. Cancer, 1994; 73(8), 2087-2098.

[31] Hollen PJ, Gralla RJ, Kris MG, Potanovich LM. Quality of life assessment in individuals with lung cancer: testing the Lung Cancer Symptom Scale (LCSS). Eur J Cancer, 1993; 29, S51-S58.

[32] Pérol M, Ciuleanu TE, Arrieta O, et al. Quality of life results from the phase 3 REVEL randomized clinical trial of ramucirumab-plus-docetaxel versus placebo-plus-docetaxel in advanced/metastatic non-small cell lung cancer patients with progression after platinum-based chemotherapy. Lung Cancer, 2016; 93, 95-103.

[33] Bohrnstedt GW. A quick method for determining the reliability and validity of multiple-item scales. Am Sociol Rev, 1969; 542-548.

[34] Wahlqvist P, Carlsson J, Stålhammar NO, Wiklund I. Validity of a Work Productivity and Activity Impairment Questionnaire for Patients with Symptoms of Gastro-Esophageal Reflux Disease (WPAI-GERD)—Results from a Cross-Sectional Study. Value Health, 2002; 5(2), 106-113.

[35] DeVellis RF. Scale development: theory and applications. Sage publications, Newberry Park, CA, 1991.

[36] Altman DG. Practical statistics for medical research. Chapman and Hall, London, 1991.

[37] Sarna L, Evangelista L, Tashkin D, et al. Impact of respiratory symptoms and pulmonary function on quality of life of long-term survivors of non-small cell lung cancer. Chest, 2004; 125(2), 439-445.

[38] Tanaka K, Akechi T, Okuyama T, Nishiwaki Y, Uchitomi Y. Factors correlated with dyspnea in advanced lung cancer patients: organic causes and what else?. J Pain Symptom Manage, 2002; 23(6), 490-500.

[39] Reddy SK, Parsons HA, Elsayem A, Palmer JL, Bruera E. Characteristics and correlates of dyspnea in patients with advanced cancer. J Palliat Med, 2009; 12(1), 29-36.

[40] American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease.Am J Respir Crit Care Med, 1995; 152, S78-S121.

[41] Nishimura K, Izumi T, Tsukino M, Oga T. Dyspnea is a better predictor of 5-year survival than airway obstruction in patients with COPD. Chest, 2002; 121(5), 1434-1440.

[42] Habraken JM, terRiet G, Gore JM, et al. Health-related quality of life in end-stage COPD and lung cancer patients. J Pain Symptom Manage, 2009; 37(6), 973-981.

[43] Gore JM, Brophy CJ, Greenstone MA. How well do we care for patients with end stage chronic obstructive pulmonary disease (COPD)? A comparison of palliative care and quality of life in COPD and lung cancer. Thorax, 2000; 55(12), 1000-1006.

[44] Bausewein C, Booth S, Gysels M, et al. Understanding breathlessness: cross-sectional comparison of symptom burden and palliative care needs in chronic obstructive pulmonary disease and cancer. J Palliat Med, 2010; 13(9), 1109-1118.

TABLES

Table 1 Demographic and clinical characteristics of the study sample (N=101)

Demographic and clinical characteristics		Number (%)
Age (year)	80-99	7 (6.9)
	60-79	80 (79.2)
	40-59	13 (12.9)
	20-39	1 (1.0)
	Mean (SD)	67.7±9.6
Gender	Female	54 (53.5)
	Male	47 (46.5)
Employment Status	Retired	59 (58.4)
	Retired for health reasons	25 (24.8)
	In paid employment	7 (6.9)
	Self-employed	2 (2.0)
	Housewife	2 (2.0)
	Long term sickness	2 (2.0)
	Disabled	2 (2.0)
	Never worked	1 (1.0)
	Not recorded	1 (1.0)
Patient ever smoked	Yes	93 (92.1)
	No	8 (7.9)
Diagnosis of COPD	Yes	39 (38.6)
	No	61 (60.4)
	Not recoded	1 (1.0)
Symptom cluster	Presence of breathlessness	99 (98.0)
	Presence of cough	81 (80.2)
	Presence of fatigue	99 (98.0)
Emotional status	Presence of anxiety (HADS-A ≥8)	32 (31.7)
	Presence of depression (HADS-D ≥8)	39 (38.6)
Treatment group status	Absence of further active antineoplastic therapy	12 (11.9)
	Post-curative treatment	37 (36.6)
	Follow-up palliative cancer care	52 (51.5)

HADS-A: Hospital Anxiety and Depression Scale-Anxiety; HADS-D: Hospital Anxiety and Depression Scale-Depression

Table 2 Associations between D-12 and NRS, HADS and LCSS

	D-12 total	D-12 physical	D-12 emotional
NRS scales			
NRS-average breathlessness	0.495[a]	0.475[a]	0.481[a]
NRS-worst breathlessness	0.514[a]	0.512[a]	0.495[a]
NRS-distress associated with breathlessness	0.611[a]	0.552[a]	0.642[a]
NRS-ability to cope with breathlessness	-0.165	-0.139	-0.131
NRS-unpleasant associated with breathlessness	0.556[a]	0.556[a]	0.555[a]
HADS			
HADS total	0.585[a]	0.465[a]	0.673[a]
HADS anxiety	0.628[a]	0.486[a]	0.706[a]
HADS depression	0.463[a]	0.390[a]	0.526[a]
LCSS total	0.551[a]	0.524[a]	0.525[a]

D-12: Dyspnoea-12; NRS: Numerical Rating Scale; HADS: Hospital Anxiety and Depression Scale; LCSS: Lung Cancer Symptom Scale

a: significant at 0.01

Table 3 Factor analysis for the D-12 items

D-12 items	Factor 1 (Physical component)	Factor 2 (Emotional Component)
D12-1 My breath does not go in all the way	**0.684**	0.221
D12-2 My breathing requires more work	**0.723**	0.345
D12-3 I feel short of breath	**0.740**	0.242
D12-4 I have difficulty catching my breath	**0.813**	0.313
D12-5 I cannot get enough air	**0.771**	0.419
D12-6 My breathing is uncomfortable	**0.759**	0.363
D12-7 My breathing is exhausting	**0.697**	0.527
D12-8 My breathing makes me feel depressed	0.317	**0.847**
D12-9 My breathing makes me feel miserable	0.302	**0.870**
D12-10 My breathing is distressing	0.460	**0.775**
D12-11 My breathing makes me agitated	0.336	**0.835**
D12-12 My breathing is irritating	0.348	**0.787**

D-12: Dyspnoea-12

Table 4 Discriminate performance of the D-12 for HADS anxiety and depression groups*

D-12 scores	Anxious (HADS-A ≥ 8)		Non-anxious (HADS-A<8)		Depressed (HADS-D≥ 8)		Non-depressed (HADS-D<8)	
	n	Mean (SE)	n	Mean (SE)	n	Mean (SE)	n	Mean (SE)
D-12 total	32	25.0(1.5)	65	13.7 (0.9)	39	23.1 (1.4)	59	13.8(1.0)
D-12 physical	28	14.3 (1.0)	61	9.3 (0.6)	33	13.7 (0.8)	57	9.3 (0.7)
D-12 emotional	32	10.7 (0.7)	63	4.3 (0.5)	38	9.7 (0.7)	58	4.4 (0.5)

All differences were statistically significant at $P<0.001$.

D-12: Dyspnoea-12; HADS: Hospital Anxiety and Depression Scale; HADS-A: Hospital Anxiety and Depression Scale-Anxiety; HADS-D: Hospital Anxiety and Depression Scale-Depression

Note: D-12 total and all subscale score differences between anxious and non-anxious patients, and D-12 total and emotional score differences between depressed and non-depressed patients were tested by Mann-Whitney U test, while D-12 physical score difference between depressed and non-depressed patients was analysed by Independent-samples t-test, based on the normality test results as measured by Shapiro-Wilk approach.

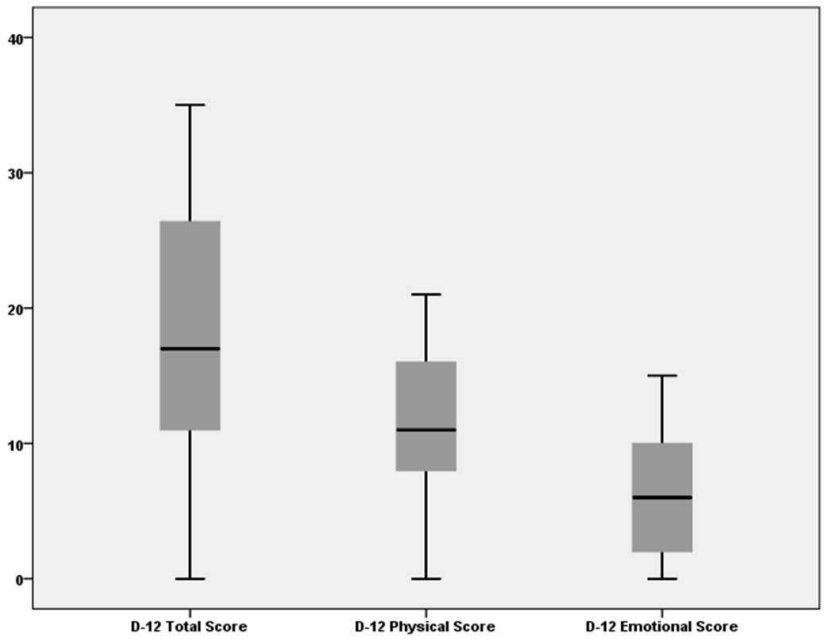
Table 5 Discriminate performance of the D-12 between patients with and without COPD

D-12 scores	COPD patients		Non-COPD patients		*P* value
	n	Mean (SE)	n	Mean (SE)	
D-12 total[a]	39	20.7 (1.5)	61	15.7 (1.1)	0.012
D-12 physical[b]	36	12.7 (0.9)	54	9.7 (0.7)	0.007
D-12 emotional[a]	37	8.0 (0.8)	60	5.6 (0.6)	0.015

D-12: Dyspnoea-12

a:Mann-Whitney U test; b:Independent-samples t-test

388 **Figure**



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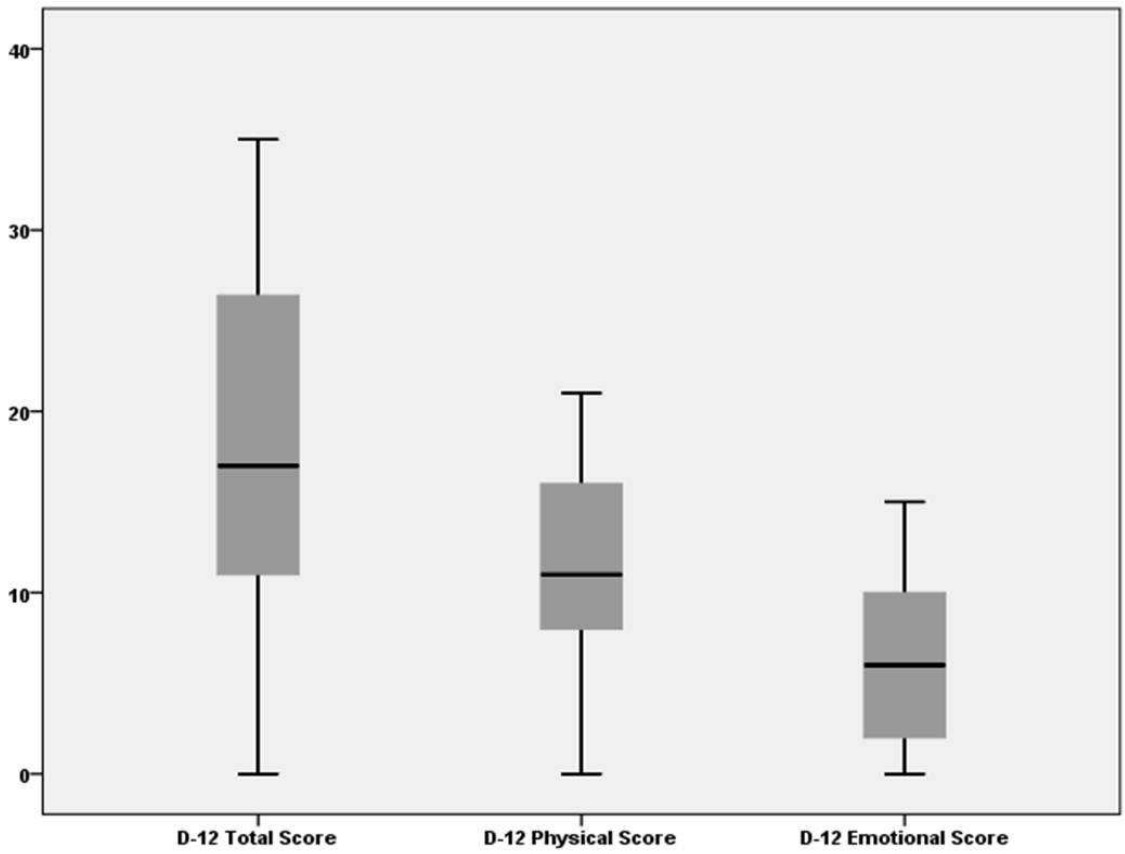
390 **Figure 1 Distribution of D-12 total and component scores**

391 D-12: Dyspnoea-12


40
30
20
10
0
D-12 Total Score
D-12 Physical Score
D-12 Emotional Score